

**Amendments to the Claims:**

1. (canceled)
2. (currently amended) The A crystal of claim 1 formed by insulin-like growth factor-1 (IGF-1) of SEQ ID NO: 1 that diffracts x-ray radiation to produce a diffraction pattern representing the three-dimensional structure of the IGF-1, and having has approximately the following cell constants  $a=31.831 \text{ \AA}$ ,  $b=71.055 \text{ \AA}$ ,  $c=65.995 \text{ \AA}$ , and a space group of  $C222_1$ , and  $\alpha=\beta=\gamma$ .
3. (currently amended) The crystal of claim 1 2 wherein the IGF-1 contains an A-, B-, C-, and D-region and forms a dimer in the crystal and wherein the crystal comprises a receptor binding site at the dimer interface.
4. (currently amended) A composition comprising the crystal of claim 1 2 and a carrier.
5. (original) The composition of claim 4 wherein the IGF-1 is biologically active when resolubilized.
6. (original) A method of treating a mammal suffering from an agonist disorder, said method comprising administering to said mammal an effective amount of the composition of claim 5.
7. (original) The method of claim 6 wherein the mammal is human.
8. (original) The method of claim 6 wherein the disorder is diabetes, obesity, a heart dysfunction, AIDS-related wasting, a kidney disorder, a neurological disorder, a whole body growth disorder, or an immunological disorder.
9. (currently amended) A method of crystallizing insulin-like growth factor-1 (IGF-1) of SEQ ID NO: 1 comprising the steps of:
  - (a) mixing an aqueous solution comprising said IGF-1 in a concentration of about 1 to 50 mg/ml with a reservoir solution comprising a precipitant selected from the group consisting of polyethylene glycol, sodium citrate, ammonium sulfate, sodium cacodylate, and a mixture thereof, to form a mixed volume; and

(b) crystallizing the mixed volume to yield IGF-1 crystals that diffract x-ray radiation to produce a diffraction pattern representing the three-dimensional structure of the IGF-1, and have approximately the following cell constants  $a=31.831 \text{ \AA}$ ,  $b=71.055 \text{ \AA}$ ,  $c=65.995 \text{ \AA}$ , and a space group of  $C222_1$ , and  $\alpha=\beta=\gamma$ .

10. (original) The method of claim 9 wherein the IGF-1 is obtained from a prokaryotic cell.
11. (canceled)
12. (original) The method of claim 9 wherein the aqueous solution of step (a) contains about 5 to 15 mg per ml of IGF-1.
13. (canceled)
14. (original) The method of claim 12 wherein the precipitant is polyethylene glycol buffered with sodium citrate or sodium cacodylate.
15. (currently amended) The method of claim ~~13~~ 9 wherein the precipitant is present in the reservoir solution in an amount of about 20 to 25% if polyethylene glycol, and about 1 to 10 M if sodium citrate, ammonium sulfate, or sodium cacodylate.
16. (original) The method of claim 9 wherein the reservoir solution further comprises a detergent.
17. (original) The method of claim 16 wherein the detergent is present in an amount of about 10 to 50 mM.
18. (original) The method of claim 16 wherein the detergent is N, N-bis(3-D-gluconamidopropyl)-deoxycholamine.
19. (original) The method of claim 9 wherein the pH of the reservoir solution is about 4 to 10.
20. (currently amended) The method of claim 9 19 wherein the pH is about 6.5.
21. (original) The method of claim 9 wherein step (b) is carried out by vapor diffusion crystallization, batch crystallization, liquid bridge crystallization, or dialysis crystallization.

22. (original) The method of claim 9 wherein step (b) is carried out by vapor diffusion crystallization.
23. (original) The method of claim 9 further comprising recrystallizing the IGF-1 after step (b).
24. (original) The method of claim 23 wherein the recrystallization takes place using methyl pentanediol.
25. (original) The method of claim 9 further comprising isolating the crystalline IGF-1.
26. (original) The method of claim 9 wherein the aqueous solution is mixed with about 24% polyethylene glycol buffered to about pH 6.5 with either about 0.1M sodium citrate or about 0.1M sodium cacodylate and about 1  $\mu$ l of about 1.4 mM N, N-bis(3-D-gluconamidopropyl)-deoxycholine detergent, this solution is equilibrated by vapor diffusion crystallization with about 1 mL of about 24% polyethylene glycol buffered to about pH 6.5 with either about 0.1M sodium citrate or about 0.1M sodium cacodylate until crystallization droplets are formed, and about 2  $\mu$ l of about 100% methyl pentanediol are added to the crystallization droplets so as to dissolve the crystals overnight and thereby form new crystals.
27. (currently amended) Crystalline insulin-like growth factor-1 (IGF-1) produced by the method of claim 9 26.
- 28-34. (canceled)
35. (currently amended) A co-crystalline complex of crystals of insulin-like growth factor-1 (IGF-1) of SEQ ID NO: 1 having approximately the following cell constants  $a=31.831 \text{ \AA}$ ,  $b=71.055 \text{ \AA}$ ,  $c=65.995 \text{ \AA}$ , and a space group of  $C222_1$ , and  $\alpha=\beta=\gamma$ , and N, N-bis(3-D-gluconamidopropyl)-deoxycholine.
36. (currently amended) A method for determining a three-dimensional structure of IGF-1 of SEQ ID NO: 1 comprising:
  - (a) crystallizing the IGF-1;

- (b) irradiating the crystalline IGF-1 to obtain a diffraction pattern characteristic of the crystalline IGF-1, wherein the crystalline IGF-1 has approximately the following cell constants  $a=31.831$  Å,  $b=71.055$  Å,  $c=65.995$  Å, and a space group of  $C222_1$ , and  $\alpha=\beta=\gamma$ ; and
- (c) transforming the diffraction pattern into the three-dimensional structure of the IGF-1.
37. (canceled)
38. (currently amended) An insulin-like growth factor-1 (IGF-1) crystal whose X-ray diffraction pattern is consistent with the three-dimensional structure structural of the crystalline IGF-1 protein of SEQ ID NO: 1 defined by the atomic coordinates shown in Appendix 1.
39. (currently amended) A method of using a three-dimensional structure of insulin-like growth factor-1 (IGF-1) derived from an IGF-1 crystal of claim 2 wherein the three-dimensional structure of IGF-1 includes an IGF-1 receptor-binding region, the method comprising identifying compounds having structures that interact with the receptor-binding region of the three-dimensional structure of IGF-1 and function as an IGF-1 agonist or antagonist.
40. (original) The method of claim 39 wherein the three-dimensional structure of IGF-1 includes alpha-carbon coordinates substantially the same as those of the structural information presented in Appendix 1.
41. (currently amended) A method of identifying insulin-like growth factor (IGF-1; SEQ ID NO: 1) agonists or antagonists comprising the steps of:
- (a) crystallizing IGF-1 to form IGF-1 crystals according to claim 2, the IGF-1 crystals containing a group of amino acid residues defining an IGF-1 receptor-binding region;
- (b) irradiating the IGF-1 crystals from step (a) to obtain a diffraction pattern of the IGF-1 crystals;

- (c) determining a three-dimensional structure of IGF-1 from the diffraction pattern, the structure including an IGF-1 receptor-binding region; and
  - (d) identifying an IGF-1 agonist or antagonist having a three-dimensional structure that functionally duplicates essential IGF receptor-binding, solvent-accessible residues presenting the three-dimensional structure of the IGF-1 receptor-binding region, said IGF-1 agonist or antagonist having altered signal transduction capacity to IGF-1-responsive cells, as compared to IGF-1.
42. (original) The method of claim 41 wherein the solvent-accessible residues do not participate in formation of the IGF-1 interface.
43. (currently amended) A method of designing a compound that mimics the 3-dimensional surface structure of the crystalline insulin-like growth factor-1 (IGF-1) of claim 2 comprising the steps of:
- (a) determining the 3-dimensional structure of the IGF-1; and
  - (b) designing a compound that mimics the 3-dimensional surface structure of the IGF-1.
44. (currently amended) A method for identifying a peptidomimetic that binds the crystalline insulin-like growth factor-1 (IGF-1) of claim 2 and blocks binding of an IGFBP or a receptor that binds to IGF-1 comprising the steps of:
- (a) searching a molecular structure database with the structural parameters or structural coordinates provided in Appendix 1; and
  - (b) selecting a molecule from the database that mimics the structural parameters or structural coordinates of the IGF-1.
45. (currently amended) A method for determining at least a portion of a three-dimensional structure of a molecular complex, said complex comprising the crystalline insulin-like growth factor-1 (IGF-1) of claim 2, and said method comprising the steps of:
- (a) determining the structural coordinates of ~~a crystal of the~~ IGF-1 crystal of claim

- 2;
- (b) calculating phases from the structural coordinates;
  - (c) calculating an electron density map from the phases obtained in step (b); and
  - (d) determining the structure of at least a portion of the complex based on said electron density map.
46. (original) The method of claim 45 wherein the structural coordinates used in step (a) are substantially the same as those described in Appendix 1 or describe substantially the same crystal as the coordinates in Appendix 1.
47. (currently amended) A method for evaluating the ability of a chemical entity to associate with crystalline insulin-like growth factor-1 (IGF-1) of claim 2 or a complex thereof,  
the method comprising the steps of:
- (a) employing computational or experimental means to perform a fitting operation between the chemical entity and the IGF-1 or complex thereof, thereby obtaining data related to the association; and
  - (b) analyzing the data obtained in step (a) to determine the characteristics of the association between the chemical entity and the IGF-1 or complex thereof.
48. (currently amended) A chemical entity identified by the method of claim 47 wherein the entity interferes with the *in vivo* or *in vitro* association between crystalline insulin-like growth factor-1 (IGF-1) of claim 2 and its receptor or between said IGF-1 and at least one of its binding proteins, or associates with a binding site on IGF-1.
49. (currently amended) A heavy-atom derivative of ~~a-crystallized form of the~~ crystalline IGF-1 of claim 2.
50. (currently amended) A method of computationally or experimentally evaluating a chemical entity to obtain information about its association with a binding site of insulin-like growth factor-1 (IGF-1) using a-crystal of an IGF-1 crystal of claim 2,

~~having the structural coordinates described in Appendix 1~~ whose X-ray diffraction pattern is consistent with the three-dimensional structure of IGF-1 protein of SEQ ID NO: 1 defined by the atomic coordinates shown in Appendix 1.